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F.Grande Covian and P.Brandt Rehberg

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Results on kidney function tests during and after heavy muscular work are discussed on the basis of a modified filtration-resorption theory, covering filtration in the glomeruli, resorption of water and of threshold substances in the tubuli, back-diffusion of diffusible substances in the tubuli. Creatinine tests and urea clearance showed that a reduction in diuresis occurred during and after muscular work, proportional to the intensity of the work done. The presumable reason is an increased resorption, due to enhanced water loss. The filtration remained constant during light and moderate work, decreased during strenuous work, and returned to normal after stopping the exercise. Proteinuria after exhausting work was attributed to an incipient renal anoxemia.

The behavior of kidney function during physical exertion has been a point of interest for a long time. However, a correct concept on the actual function mechanism of the kidneys during physical work cannot be obtained from available literature data. This is due to the fact that only a few of the earlier authors made true function tests and were usually satisfied with urinalyses.

More recently, various papers were published (Addis and Drury, 1923; McKay,

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** Numbers in the margin indicate pagination in the original foreign text.

1928; van Slyke, Alving, and Rose, 1932) on studies of kidney function based on urine excretion. Addis and Drury as well as McKay found a decrease in urea clearance, while van Slyke and coworkers, at moderately heavy work, observed no distinct decrease; they found a drop in the clearance values only after exhausting work.

The results of the above authors are difficult to evaluate since they did not measure the work output and since the type of work differed. Addis and Drury made their determinations after a one-hour run, McKay after two hours tennis playing, and van Slyke after stair climbing or, in some cases, after "racket squash".

In our work, we investigated the kidney function before, during, and after an accurately proportioned work.

As basis for our investigation, we used the filtration-resorption theory, modified by us (Rehberg, 1926; Holten and Rehberg, 1931). According to this theory, the processes taking place in the kidneys - disregarding synthetic processes - are as follows:

1) Filtration in the glomeruli; /22

2) Resorption of water and threshold substances in the tubuli;

3) Back-diffusion of diffusible substances in the tubuli.

An investigation of the kidney function must thus encompass a study of filtration, resorption, and back-diffusion.

According to Rehberg, creatinine excretion is a criterion for the filtration, under the assumption that the creatinine is filtered by the glomeruli and that all of the filtered creatinine appears in the urine. Thus, we have: filtration per minute = degree of concentration of the creatinine, multiplied by diuresis per minute or $F = C \cdot D$, where C (concentration index) =

$$= \frac{\text{urine creatinine concentration}}{\text{blood creatinine concentration}}.$$

The degree of water resorption is given by the concentration index.

The back-diffusion is investigated by a comparison of urea excretion and creatinine excretion. From the calculated filtration and the blood urea, the amount of urea filtered per minute can be computed. The greater the back-diffusion in the tubuli the smaller will be the percentage ($E_u\%$) of this amount that actually appears in the urine. This percentage (excretion percent) $E_u\%$ is equal to $\frac{\text{diuresis} \times \text{urine urea} \times 100}{\text{filtration} \times \text{blood urea}}$ or $\frac{Cu}{C_{cr}} \times 100$ where Cu and C_{cr} denote the concentration indices for urea and creatinine.

The back-diffusion of urea depends on the degree of concentration of the urine; the more the urine is concentrated the more urea will be back-diffused during the concentration prooess.

To facilitate a comparison with the terminology of other investigators, we also entered the values of "urea clearance" or "clearance" in our Tables. This term indicates the amount of blood containing the same amount of urea excreted in one minute* (Møller, McIntosh, and van Slyke, 1928).

1. Experimental Setup

Our experiments were made on two normal male test subjects whose occupation was ordinary laboratory work. One of these, O.B. (27 yrs, 1.85 m, 77 kg) was in excellent training while the other F.G.C. (24 yrs, 1.78 m, 74 kg) was less well trained and hardly was active in athletics. All experiments were made on the Krogh bicycle ergometer. The work intensity was varied from 720 to 1620 kg-m/min, while the working period was kept constant within the individual

* Urea clearance = the volume of the blood which is cleared of urea per minute by renal elimination (Transl.).

experimental days. The duration of the work was one hour for O.B., except /23
for the work of 1620 kg-m/min during which he exercised for only 30 min. For F.G.C., the experimental period was one hour for 720 and 900 kg-m/min; 40 min for 1080 kg-m/min; 20 min for 1260 kg-m/min; and 12 min for 1440 kg-m/min. The determination of diuresis, during these latter short-time tests, was rather unreliable. The rate of work was kept constant at 64 pedal revolutions per minute. The temperature in the testing room was about 20°C in all experiments. The test subjects wore only swim trunks during the exercise.

Below, we give a typical example of one experimental run:

8 A.M.	Test subject (in the fasting state) drinks 5 gm creatinine in 500 cc water;
9 A.M.	Test subject urinates; first blood test followed by rest until 10 A.M.;
10 A.M.	First urine test, second blood test; subject is weighed and work is started;
11 A.M.	End of work, second urine test, third blood test; subject is weighed again and is allowed to rest until 12 noon;
12 Noon	Third urine test and fourth blood test.

If the working period did not last one full hour, urine and blood tests were made immediately after stopping the work. The rest period always was one full hour and the test subject remained in a sitting position so as to prevent any effects produced by a change in position. Control tests were made repeatedly, in which the subject remained seated for three hours, with samples taken every hour. The amount of water ingested by the subjects was so selected that they had an almost constant diuresis during the three-hour rest experiments. During the exercise itself, pulse and blood pressure were frequently determined.

2. Methodics

The creatinine determinations in the urine were performed according to the Holten and Rehberg method. The blood creatinine was determined as follows: A total of 0.2 or 0.4 cc blood was mixed in a centrifuge glass with 1 cc distilled water, to which 2 cc saturated picric acid solution and an excess of solid picric acid were added. The solution was thoroughly mixed and shaken, left standing for 30 min, and then centrifuged for 15 min; 2 cc liquid were pipetted off and, in a small test tube, mixed with 0.1 cc 10% $NaOH$ and 0.1 cc dist. /24
water; after shaking, the mixture was left standing for 25 min and then compared in the Bürker colorimeter. The standard solution is prepared with 2 cc saturated picric acid solution + 0.1 cc 10% $NaOH$ + 0.1 cc creatinine standard solution which contains 10 mg creatinine per 100 cc.

The method was checked in parallel tests with the Folin method, in the form prescribed by Holten and Rehberg, showing excellent agreement.

To confirm the uniform distribution of the creatinine between blood corpuscles and plasma, we made parallel determinations with both methods on whole blood and serum.

A typical example is as follows:

	Folin	Picric Acid Precipitation
Whole blood	7.02 mg%	7.35 mg%
Serum	7.30 mg%	7.15 mg%

The urea determinations were made with a urease method. The formed ammonia was expelled by vacuum distillation in a modified Parnas apparatus and titrated with a microburette*.

* The urea determinations were made by C.Blem.

In numerous experiments, the protein content of the plasma was determined with a Pulfrich immersion refractometer.

3. Results

To facilitate presentation of the results, we arranged them in tabular form.

In the Tables, the values for diuresis (D), filtration (F), and clearance (Cl) are always expressed in cc/min, the concentration of urea and creatinine always in mg%, and the excretion of creatinine in mg/min. No corrections for body surface are made; however, to permit a possible comparison with other results, we also indicated, at the top, the weight and height of our test subjects.

a) Experiments at Rest

To determine the normal fluctuations in the renal function of our test subjects, we made a number of experiments at rest, which indicated that the filtration, in the subject F.G.C., fluctuated between 106 and 228 cc/min. The mean value was 156 cc, with a scattering of ±22.6 (40 observations). The /25
corresponding figures for O.B. are: mean value of filtration, 149 cc/min with a scattering of ±18.8 (19 observations).

Therefore, as the lowest limit of normal filtration we can consider a value of 88 cc for F.G.C. and of 93 cc for O.B.

The scattering values, given in this article, were calculated according to the formula $1.253 \times \frac{\Sigma d}{\sqrt{n}(n-1)}$ where d corresponds to the difference between the individual observations and the mean value of the various observations.

Curve 1 shows the filtration values as a function of the diuresis, observed during the rest periods. In agreement with the theory, it was found that the filtration (creatinine excretion) is largely independent of the diuresis. Therefore, in any comparison of different filtration values, the diuresis can be disregarded.

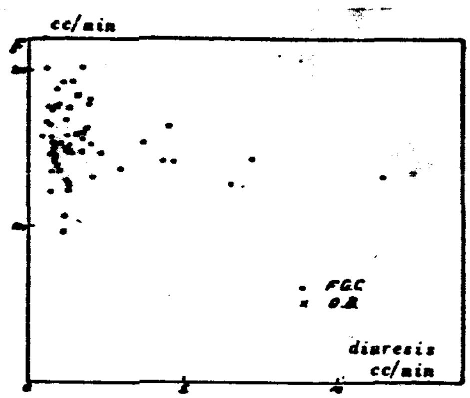

Fig.1 The Diagram Shows the Considerable Independence of the Filtration from the Diuresis
In all diuresis values, the filtration fluctuated within the same limits.

In the test subject F.G.C. who had ingested relatively large quantities of water in some of the experiments, the diuresis fluctuated within wide limits (0.46 - 12.40 cc/min), while in the test subject O.B., it fluctuated only little (0.34 - 1.90 cc/min).

The concentration index, which represents a criterion for the water resorption in the tubuli, fluctuated in the subject F.G.C. - in accordance with the variable diuresis - between 10.8 and 343, while the same value for the subject O.B. was only 85.5 to 194.

Since, as is generally known, urea excretion depends largely on the diuresis, it is necessary to allow for the extent of diuresis in comparing the degree of urea excretion in various experiments. To establish a law for this dependence, various formulas were derived. The most popular are the standard and maximum clearance formulas established by van Slyke and coworkers. However, /26 at fluctuations in diuresis about 2 cc/min, it is difficult to determine which of the two formulas should be used.

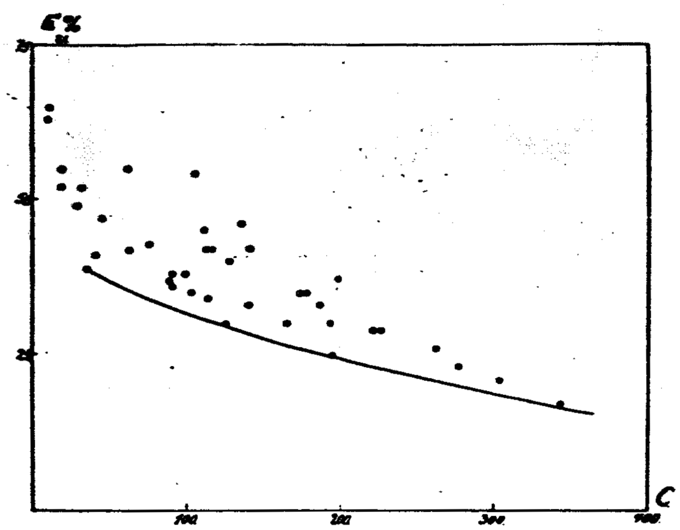

Fig.2 Dependence of the E_u% (Percentage of the Filtered Actually Excreted Urea) on the Degree of Urine Concentration
(C = Concentration Index for Creatinine)
Test subject F.G.C.; the line is to indicate the empirically determined lower limit

In a still unpublished report, Holten and Rehberg gave a computation method according to which a formula can be established that is valid for all diureses.

The clearance values found for the subject F.G.C. thus correspond to the formula $Cl = \frac{100 \cdot V}{1.09\,V + 0.87}$, where V gives the diuresis per minute. Compared with this formula, the values show a scattering of +13.7% so that clearance values less than 59% of the value derived from this formula must be considered subnormal.

For the subject O.B., the found values correspond to the formula Cl = /27
$= \frac{100\,V}{1.15\,V + 0.93}$, with a scattering of ±9.4%. Thus, the normal lower limit is 72% of the value calculated from the formula.

According to the theory, the dependence of the urea excretion on the diuresis has its cause in the fact that the filtered urea, during the concentration process in the tubuli, partly back-diffuses through the tubule walls. The more concentrated the urine becomes, the greater are the quantities diffused back and the less will be the actual excretion. The "excretion percent" = E_u% becomes small.

If the values, found in the subject F.G.C., are plotted as a function of the concentration index (C), we will find (Fig.2) that E_u% decreases with increasing C. At low urine concentration (10), about 65% of the filtered urea are excreted so that approximately 35% are back-diffused during the concentration processes. At a high degree of concentration, this back-diffusion is much greater, and only 20% of the filtered urea are contained in the total urine, at C = 300. The values shown by O.B. fall within such a narrow concentration range that this tendency is not clearly defined.

b) <u>Work and Restitution</u>

1. Tables 1 and 2 give a compilation of the results of the filtration determinations during working experiments and subsequent restitution periods.

Of the 38 filtration values, determined during the work, only three are below the lower normal limits, while ten determinations or 26% are below the limits at which only 5% should have been expected; a comparison with the preceding rest periods will always show a distinct decrease in the filtration. Only at a work intensity of 1260 kg-m/min for the subject F.G.C. and of 1440 kg-m/min for the subject O.B. does this decrease become significant.

All of the restitution values are within the normal limits and, compared with the preceding rest periods, rather show a slight rise.

The mean values of work and restitution filtrations, at the various work intensities, are plotted for both test subjects in Fig.3, in percent of the

TABLE 1

FILTRATION IN THE WORK TESTS WITH F.G.C.

No.	Load kgm/m	Filtration			Work filtration in % of rest value	Restitution value in % of rest value
		Rest	Work	Restitution		
1	720	165	126	144	77	87
2	"	148	142	142	96	96
3	"	127	101		80	
4	"	131	98		75	
5	"	188	138		74	
6	"	196	170	167	87	85
7	"	160	166		104	
8	"	145	151		104	
9	"	150	169		113	
10	900	122	124	148	102	121
11	"	135	153	170	113	126
12	"	130	116	140	89	108
13	"	106	147		139	
14	1080	141	128	132	91	94
15	"	129	133	145	103	104
16	"	148	134	186	91	126
17	1260	178	96	155	54	87
18	"	152	66	166	43	[illegible]
19	"	148	131	138	89	[illegible]
20	"	193	120	145	62	75
21	"	157	130	193	83	123
22	"	202	137	242	68	120
23	1440	173	91	161	53	93
24	"	228	142	209	62	92

Lower normal limit of filtration: 88 cc.

TABLE 2

FILTRATION IN THE WORK TESTS WITH O.B.

No.	Load kgm/m	Filtration			Work filtration in % of rest value	Restitution value in % of rest value
		Rest	Work	Restitution		
1	720	184	143	140	78	76
2	"	127	155	155	122	122
3	900	135	129	160	96	118
4	"	159	117	140	74	88
5	"	163	141	132	87	81
6	"	153	155	149	101	97
7	1080	147	136	168	93	114
8	"	139	136	164	97	118
9	1260	123	114	182	93	148
10	"	96	91	140	95	146
11	1440	176	102	172	58	98
12	"	147	107	158	73	107
13	1620	206	95		46	
14	"	159	39		25	

Lower normal limit of filtration: 93 cc.

preceding rest values.

2. The diuresis is almost always reduced and, in strenuous work, is very much lowered. This decrease takes place even if large quantities of water had been ingested before the test. Also during the restitution periods, the diuresis - at least if the preceding work had been exhausting - is almost always reduced. The mean values are given in Fig.4. /29

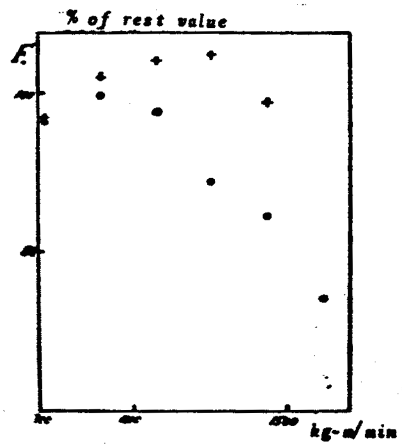

Fig.3 Filtration during Work and Restitution Periods, in Percent of the Preceding Rest Values
• Work + restitution; the values given here and in Figs.4, 5, and 6 are mean values of determinations on both test subjects.

3. The concentration index rises in most cases, occasionally showing a decrease but always followed by a further increase during the restitution

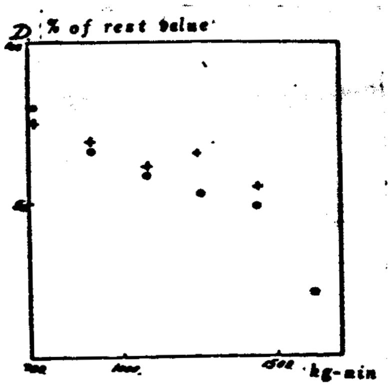

Fig.4 Diuresis in the Work and Restitution Periods, in Percent of the Preceding Rest Values
• Work + restitution.

TABLE 3

UREA EXCRETION IN THE WORK TESTS WITH F.G.C.

Calculated clearance			*Found value in percent of calculated*		
Rest	*Work*	*Restitution*	*Rest*	*Work*	*Restitution*
65.1	46	48.3	101	88	90
46	46	49.5	107	100	95
82	79.9		80	63	
85.7	77.3		99	67	
54.5	39.7		86	81	
43.3	42.2	43.7	123	106	82
44	39.7	45.3	83	72	81
44.7	45.3	46.9	105	90	84
68.3	54.2	48.6	105	79	86
54.7	39.5		105	49	
46.9	37.8	40.4	126	90	107
56.6	44	46.6	88	72	118
57.1	40	43.3	116	84	98
51.1	33.6	46.6	120	59	87
57.3	42.2	45.7	89	43	62
56.3	51.1	52.2	111	82	100
58.7	32.6	40.4	108	49	82
45.7	34.1	45	126	66	115
63	58	60.7	135	72	95
49.7	30.2	38.6	127	59	87
45	44	44.4	119	66	92

Normal lower limit of the found clearance: 59%.

TABLE 4

UREA EXCRETION IN THE WORK TESTS WITH O.B.

Calculated clearance			*Found value in percent of calculated*		
Rest	*Work*	*Restitution*	*Rest*	*Work*	*Restitution*
57.8	43.6	43.8	90	93	88
47.1	49.3	42.3	92	81	91
48.4	38.2	41.6	97	121	92
59.3	41.1	38.6	100	104	114
60.9	50.7	43.8	88	81	85
49.1	43.6	42.3	87	97	82
53.5	41.1	38.6	106	102	105
46.8	37	35.7	101	78	91
47.1	30.6	30.6	130	69	93
50.2	28.2	27.8	99	75	99
54.1	27.8	30.6	106	63	96
59.1	31	30	104	72	87
57.2	19.3		107	71	

Normal lower limit of the found clearance: 72%.

periods. Specifically the test subject O.B. showed high concentrations during the restitution periods (to more than 400).

4. The figures of urea excretion (Tables 3 - 4), during the work as well as during the restitution periods, show a drop in the "clearance" values which were lower at all work intensities. The urea excretion itself will be discussed later in the text.

5. During the most intense work (1620 kg-m/min for O.B. and 1440 kg-m/min for F.G.C.), albumin is excreted in the urine; the amounts were considerable /31 in the subject O.B. and negligible in the subject F.G.C.

4. Discussion

Let us now turn to the question as to the cause of the changes in kidney function, found by us.

1. Filtration. The factors that determine the degree of filtration in the glomeruli are principally two, namely, 1) filtration pressure, i.e., the difference between blood pressure in the glomeruli and colloido-osmotic pressure of the plasma, 2) the blood stream. It is sufficiently well known that these factors undergo extensive changes during muscular work, so that the literature data need not be discussed here. Since an increase in blood pressure occurs during almost any muscular work, it could be expected that the filtration would also increase during work. However, we found that the filtration remains relatively constant at light to moderate work and steeply decreases during heavy work. This should indicate that the increased blood pressure does not become effective as filtration pressure and that the explanation must be looked for in a thickening of the blood which would increase the colloido-osmotic pressure and also in an incipient contraction of the afferent renal vessels during even

light work. In several of our experiments, an increase in serum protein was detected by refractometer. This hemoconcentration, in our opinion, is produced by two mechanisms: First, the water secretion during work is much greater than normal. In each experiment, we determined the amount of water secreted through lungs and skin by weighing and correcting the expired carbon dioxide.

The mean values of these determinations are as follows:

Work intensity kg-m/min	Water loss, in cc/min	
	F.C.G.	O.B.
720	8.5	—
900	10.0	6.7
1080	11.6	9.4
1260	15.0	12.6
1440	20.8	16.2
1620	—	21.3

As indicated in the above Table, the extrarenal water secretion increases /32 parallel with the intensity of work, which is readily explained by the increased ventilation and the onset of heat regulation.

Another factor which also may participate in this hemoconcentration is the increased binding of water by the muscles.

That an increased binding of water in the muscle takes place during muscular exertion was demonstrated already by Ranke (1865). Recently, other authors (Cook, 1898; Fletcher, 1904) obtained similar results in experiments on isolated frog muscles. Of special interest in this respect is the work done by Hill and Kupalov (1930). These authors found that the water-binding power of the muscle by far exceeds the osmotic changes, calculated for familiar chemical processes. Therefore, a relatively large amount of water must be taken up by the muscles themselves during muscular exertion. This fact had been recognized not only by Ranke but also by Asher and Bruck (1906) as well as by Wüscher (1925), as representing a factor for decreasing the diuresis. As a consequence, of these two mechanisms, hemoconcentration takes place.

Despite the fact that such a hemoconcentration can be held responsible for the absence of a rise in filtration during light work, it cannot be considered the determining factor for the considerable decrease in filtration during heavier work. Therefore, it must be assumed that the renal vessels contract strongly.

The literature contains data on a vasoconstriction in the splanchnic nerve region during muscular work; according to McKeith and coworkers (1923), this vasoconstriction also takes place in the renal vessels. At heavier work, the exercised muscles require increasing amounts of blood so that the circulation for the kidneys gradually decreases, causing a filtration by up to 25% of its normal value. Very soon after terminating the work, it must be assumed that the vasoconstriction in the kidneys is followed by a dilatation of the vessels, caused by a type of "reactive hyperemia". This might furnish an explanation for the fact that the filtration, after work and during the restitution period, rapidly increases to normal or higher despite the fact that the central blood pressure is reduced during this period.

2. Diuresis. The majority of literature data on diuresis during physical work (Ranke, 1871; Garrat, 1898; Asher and Bruck, 1906; Wüscher, 1925; Weber, 1926; McKeith, Pembrey, et al., 1923; Wilson, Long, et al., 1925; Dobreff, 1926; Zuntz and Schumburg, 1901) agree in the findings that, during physical work, /33 the diuresis decreases. The only exceptions here were Zuntz and Schumburg who, for unexplained reasons, encountered an increase in diuresis.

The reduction in diuresis was a constant phenomenon in our experiments. The mean values of all determinations are plotted in Fig.4. As the main cause of this reduction, the above-discussed hemoconcentration must be accepted.

Another substantiation for this concept is the fact that the decrease, except for the heaviest work, is accompanied by normal filtrations. Therefore, the decreased diuresis must be due in these cases to an increased resorption of the work.

The mechanism that stimulates the tubuli cells to an increased activity is still unknown. Vasomotor disorders, assumed by earlier authors as the true cause of decreased diuresis, are not in question at moderate work in our opinion since the vasomotor disorder cannot be reconciled with a normal filtration. Naturally, in our long experiments, it was impossible to decide whether a vasoconstriction might exist at the beginning of the exertion and rapidly disappears thereafter. At least, after stopping the work, vasomotor disorders are highly improbable. Nevertheless, the diuresis remains low which agrees best with the assumption that this reduction is a reaction of the kidney to the thickening of the blood.

3. In most cases, the concentration index rises, which agrees well with the assumption of an increased re-resorption. In very few cases in which the concentration index drops, a possible explanation might be the assumption that the oxygen supply of the kidney had been insufficient to permit the work of concentration.

4. The excretion of urea, as mentioned above, is strongly reduced during the working periods as well as during the restitution periods, compared with the rest periods (Fig.5).

However, to evaluate this reduction it is necessary to check whether this might be greater than expected from the reduced diuresis alone. To investigate this situation, the obtained clearance values must be compared with the values calculated from our earlier formulas. Such a comparison indicates that the obtained values for the working periods are almost always too low and that many of these data are entirely outside the error limit. As mean value (Fig.6), we found that at work intensities up to 1080 kg-m/min approximately 85% of the /34

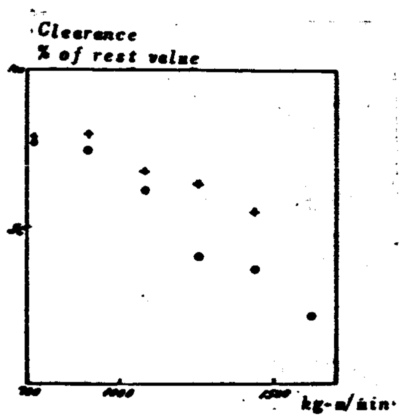

Fig.5 Urea Excretion during Work and Rest Periods, in Percent of the Preceding Rest Values
• Work + restitution.

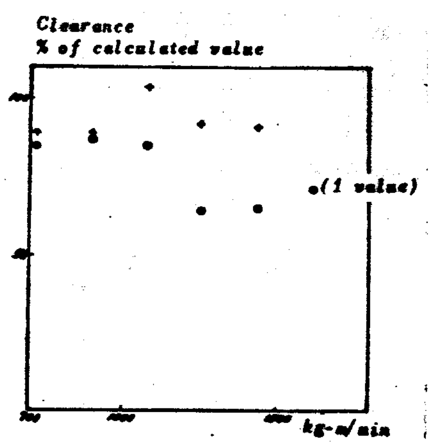

Fig.6 Urea Excretion during Work and Restitution Periods, in Percent of the Values Calculated from the Extent of Diuresis
• Work + restitution.

expected quantities are excreted whereas at heavier work, only about 65% are excreted. Thus, the reduction in urea excretion during work is too great for being attributed solely to the decreased diuresis. However, also the filtration is reduced in this case, meaning if the filtration theory is correct - as we assume here - the filtration decrease must lead also to a reduction in urea excretion. To eliminate the influence of this factor, it must be investigated whether the urea becomes as greatly concentrated during the working periods as should be expected on the basis of the degree of concentration of the creatinine. This is done by a comparison of the excretion percents (E_u%) with the normal values. /35

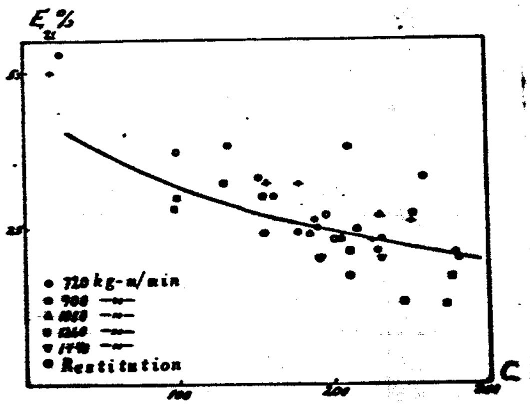

Fig.7 E_u% in the Test Subject F.G.C. during Work
The solid line indicates the lower limit of the normal values (see Fig.2).

Unfortunately, this comparison can be made only for the test subject F.G.C. since the determinations on the subject O.B., during work and rest, appear at so many different points of the curve that no reliable interpretation is possible.

In Fig.7, the values obtained during work (and restitution) are plotted. It is obvious that, at work intensities of 1080 kg-m/min and more, most of the points come to lie below the normal limit. Therefore, the urea excretion is even more reduced in these cases than would be expected from the reduced filtration and the lowered diuresis. The back-diffusion is more extensive than normally. We believe that this can be attributed to a reduction in blood circulation. The decrease in filtration can be interpreted as a change-over of the circulation to the working muscles; we believe that, during strenuous work, the reduction in circulation becomes so great that a renal anoxemia might occur, leading to an increase in the permeability of the tubule cells so that they become unable to retain the concentrated urea to the same extent or as completely as is normally the case. Such an anoxemia would also explain the albuminuria observed during maximum work, which we consider a symptom of abnormally permeable glomeruli.

During the restitution periods, the figures for the urea excretion are all within the values expected according to a calculation from the diuresis. The /36
excretion percentage is distinctly reduced in both cases. Presumably, in the one case an erroneous determination of the filtration (242) was involved, while the other case was based on an experiment in which the greatest decrease in filtration was observed during work (43% of the rest values). The decrease in renal circulation, responsible for this excessive reduction, thus has an influence on the urea excretion even during the restitution period.

The author wishes to express his thanks to Prof. A.Krogh and Dr. Hohwü Christensen for their accommodating assistance and advice. Appreciation is expressed also to Dr. O.Bøje for his cooperation as a test subject.

5. Summary

1. The behavior of kidney function during and after work is investigated by means of the creatinine method and the urea clearance determination.

2. During and after muscular work, a decrease in diuresis was observed in all cases. This reduction runs parallel with the intensity of the work done. As cause of the reduced diuresis, primarily an increase in resorption must be assumed. This increased resorption presumably is due to a greater water loss.

3. The filtration remains constant during light and moderate work, while it is increased during more strenuous work.

After stopping the work, the filtration returns to normal.

4. During very strenuous exertion - presumably as a consequence of anoxemia - protein is excreted in the urine.

5. The urea clearance is reduced already at light work, proportionally to the intensity of work. The reduction in clearance is produced in part by a decrease in diuresis and filtration and in part by an increased back-diffusion of urea which, presumably, is due to an incipient anoxemia.

6. The mechanism of these phenomena and its explanation by a modified filtration-resorption theory are discussed.

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